Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Respiratory Medicine 181 (2021) 106391

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: http://www.elsevier.com/locate/rmed

Short communication

Decreased quality of life and spirometric alterations even after mild-moderate COVID-19

Alberto Ordinola Navarro [a], Javier Cervantes-Bojalil [a], Orestes de Jesús Cobos Quevedo [a], Andrea Avila Martínez [a], Carlos Alberto Hernández-Jiménez [a], Esperanza Pérez Álvarez [a], Andrea González Gil [a], Ana Lilia Peralta Amaro [a], Olga Vera-Lastra [a], Bruno Ali Lopez Luis [b,*]

[a] Department of Internal Medicine, Hospital de Especialidades "Dr. Antonio Fraga Mouret", Centro Médico Nacional La Raza Del Instituto Mexicano Del Seguro Social, Mexico City, Mexico
[b] Department of Internal Medicine, Hospital General de Zona No.27 Del Instituto Mexicano Del Seguro Social, Mexico City, Mexico

ARTICLE INFO

Keywords:
COVID-19
Pulmonary Rehabilitation
Post-COVID
Quality of life
Respiratory infection
SARS

ABSTRACT

Background: The follow-up of recovered COVID-19 patients is still limited. We aimed to evaluate the changes in quality-of-life (QOL) and spirometric alterations in the convalescent phase of 115 patients with at least 30 days post-COVID-19.
Methods: We included patients with confirmed COVID-19 infection, available past medical records and at least 30 days after the onset of symptoms. All patients were asked to rate their general health condition before and after COVID-19 using the EQ-5D-5L standardized questionary and perform a spirometry at evaluation.
Results: In this study, that included 70%(81/115) of patients with mild or moderate COVID-19; there was a severe decrease in QOL up to 56%(64/115). Alterations in usual activities and anxiety/depression were present in 59% of patients with a severe decrease in QOL. The persistence of symptoms was present in 63%(72/115). Restrictive lung impairment was the most common spirometric alteration in 17%(20/115), of whom 65%(13/20) had mild COVID-19.
Conclusions: Spirometric alterations are presented even in mild COVID-19, and more remarkably, there is a high rate of alterations in quality of life after the recovery of this disease.

1. Introduction

The world has been affected by the biggest pandemic in recent years, coronavirus disease 2019 (COVID-19), of which we are learning through extensive research during the last months. The follow-up of post-COVID-19 patients is still limited, but the persistence of symptoms early after the disease has already been described [1]. Moreover, coronavirus infections have been reported as a cause of altered lung function, mostly related to the disease severity [2]. This study aimed to evaluate the changes in quality-of-life (QOL) and spirometric changes in the early convalescent phase of a group of recovered COVID-19 patients.

2. Methods

This follow-up study included patients evaluated for COVID-19 in The Hospital de Especialidades "Dr. Antonio Fraga Mouret," Centro Médico Nacional La Raza, México, between Apr 01 to Jul 30, 2020. The local ethics committee approved this study (registration number, R-2020-3501-158). Informed consent was obtained from all participants. The inclusion criteria were as follows: (1) Confirmed COVID-19 infection by SARS-CoV-2 real-time qPCR using nasopharyngeal swaps. (2) Available past medical records and the radiological evaluation with chest computed tomography scan (CT). (3) Patients with at least 30 days after the onset of symptoms until the time of the spirometric evaluation. Patients with baseline lung disease were excluded from the study.

Spirometry was done using a portable spirometer (MIR Spirolab®). The performance and acceptability criteria were based on ATS-ERS guidelines [3]. Normal spirometric was defined as no airflow obstruction, FEV1/FVC $\geq$0.7 with FVC $\geq$80% of the predicted values, according to NHANES III. Restrictive pattern was diagnosed as an FVC <80% of the

* Corresponding author. Hospital General de Zona No.27, Instituto Mexicano del Seguro Social, Prol, Lerdo 311, Tlatelolco, Cuauhtémoc, 06900, Mexico City, Mexico.
E-mail address: bruno_lopez@comunidad.unam.mx (B.A. Lopez Luis).

https://doi.org/10.1016/j.rmed.2021.106391
Received 9 November 2020; Accepted 31 March 2021
Available online 14 April 2021

Table 1
Baseline characteristics, spirometric interpretation, persistent symptoms and health state alterations of convalescent COVID-19 patients according to QOL.

Characteristics of patients	All patients (n = 115)	Severe decrease in QOL (n = 64)	No decrease in QOL(n = 51)	*P*-value
Age, median, (IQR), years	40 (33–48)	40 (35–47)	40 (29–53)	0.95
Sex, female	65 (57)	37 (58)	28 (55)	0.9
Comorbidities				
Active Smoker	29 (25)	17 (27)	12 (24)	0.87
Smoking Index, median (IQR)	5 (5–5)	5 (5–5)	5 (5–5)	0.87
Diabetes	16 (14)	8 (13)	8 (16)	0.82
Hypertension	16 (14)	9 (14)	7 (14)	1
Physical Examination				
BMI, median, (IQR) kg/m2	27.76 (25.37–31.46)	28.10 (25.53–31.55)	27.69 (24.76–31.24)	0.31
<25 kg/m2, No, (%)	23 (20)	11 (17)	12 (24)	0.54
25–30 kg/m2, No, (%)	56 (49)	32 (50)	24 (47)	0.9
>30 kg/m2, No, (%)	36 (31)	21 (33)	15 (29)	0.85
COVID classification[a]				
Mild	43 (37)	22 (34)	21 (41)	0.57
Moderate	38 (33)	25 (39)	13 (25)	0.18
Severe and critically ill[b]	34 (30)	17 (27)	17 (33)	0.55
Site of hospitalization				
General Ward	26 (23)	12 (19)	14 (27)	0.37
ICU	5 (4)	3 (5)	2 (4)	1
Ambulatory	84 (73)	49 (77)	35 (69)	0.45
Invasive mechanical ventilation	5 (4)	3 (5)	2 (4)	
CT Scan No, (%)				
Normal CT	29 (25)	14 (22)	15 (29)	0.47
Typical COVID-19 findings				
Unilateral GGOs	19 (17)	14 (22)	5 (10)	0.27
Bilateral GGOs	17 (15)	8 (13)	9 (18)	0.21
Unilateral consolidation	5 (4)	5 (8)	0 (0)	0.14
Bilateral consolidation	8 (7)	5 (8)	3 (6)	1
Unilateral GGOs and consolidations	4 (3)	2 (3)	2 (4)	0.62
Bilateral GGOs and consolidations	14 (12)	8 (13)	6 (12)	0.86
Nonspecific COVID-19 findings[c]				
Interlobular Septal Thickening	31 (27)	14 (22)	17 (33)	1
Bronchial wall thickening	9 (8)	4 (6)	5 (10)	1
Nodule or lymphadenopathy	5 (4)	2 (3)	3 (6)	1
Pleural or pericardial effusion	3 (3)	2 (3)	1 (2)	0.58
Days until evaluation, (mean ± SD)	58 ± 18	59 ± 18	58 ± 19	0.71
Spirometry Interpretation				
Normal	95 (83)	49 (77)	46 (90)	0.08
Restrictive pattern	20 (17)	15 (23)	5 (10)	
Spirometry Testing (mean ± SD)				
Oxygen Saturation (Fio2 21%)	94 ± 2.3	94 ± 2.49	94 ± 2.08	0.91
FEV1%	96 ± 12	93 ± 12	98 ± 12	0.33
PEF%	103 ± 19	101 ± 18	106 ± 20	0.2
FEF 25–75%	107 ± 25	103 ± 22	112 ± 28	0.07
FVC%	93 ± 14	92 ± 15	92 ± 12	0.14
FEV1/FVC%	97 ± 10	96 ± 10	98 ± 9	0.51
EQ-5D-5L No, (%)				
Mobility	31 (27)	25 (39)	6 (12)	0.43
Self-care	9 (8)	7 (11)	2 (4)	1
Usual activities	44 (38)	38 (59)	6 (12)	0.04
Pain/Discomfort	69 (60)	50 (78)	19 (37)	0.99
Anxiety/Depression	60 (52)	36 (56)	24 (47)	0.01
Persistent Symptoms No(%)[d]	72 (63)	42 (66)	30 (59)	0.57
Dyspnea	36 (50)	20 (48)	16 (53)	0.99
Headache	11 (15)	6 (14)	5 (17)	1
Pleuritic pain	14 (19)	7 (17)	7 (23)	0.77
Cough	7 (10)	3 (7)	4 (13)	0.45
Fatigue	18 (25)	13 (31)	5 (17)	0.18

Abbreviations: BMI, body mass index; CT, computed tomography; GGOs, ground-glass opacity; IQR, Interquartile range. QOL, quality of life; EQ-5D-5L, European Quality of Life-5 Dimensions-5 levels.

[a] According to COVID-19 guidelines released by the National Health Commission of China.

[b] Twenty-nine patients were classified with severe disease and five critically ill. The distribution was as follows: Decreased QOL group, 14 severe and 3 critically ill patients. No decreased QOL, 15 severe and 2 critically ill patients.

[c] Of the reported atypical findings; 19 Interlobular septal thickenings, 6 bronchial wall thickening, 1 nodule, 1 lymphadenopathy and 2 pleural effusion were presented together typical CT findings as well.

[d] Fourteen patients presented with at least two symptoms.

predicted value and an FEV1/FVC ratio >70%.

All patients were asked to rate their general health condition before and after COVID-19 disease as well as symptoms persistence at the time of the evaluation using a standardized questionary. In order to evaluate QOL, the EQ-5D-5L instrument was used [4]. It consists of a visual analogue scale from 0 (worst health) to 100 (best health) and five items: mobility, usual activities, self-care, pain/discomfort and anxiety/depression. We defined a severe decline in QOL as a decrease ≥10 points in the EQ-5D-5L visual analogue scale.

Qualitative variables were presented as proportions and quantitative variables as mean (standard deviation) or medians (interquartile range) when appropriate. Statistical comparisons were performed between

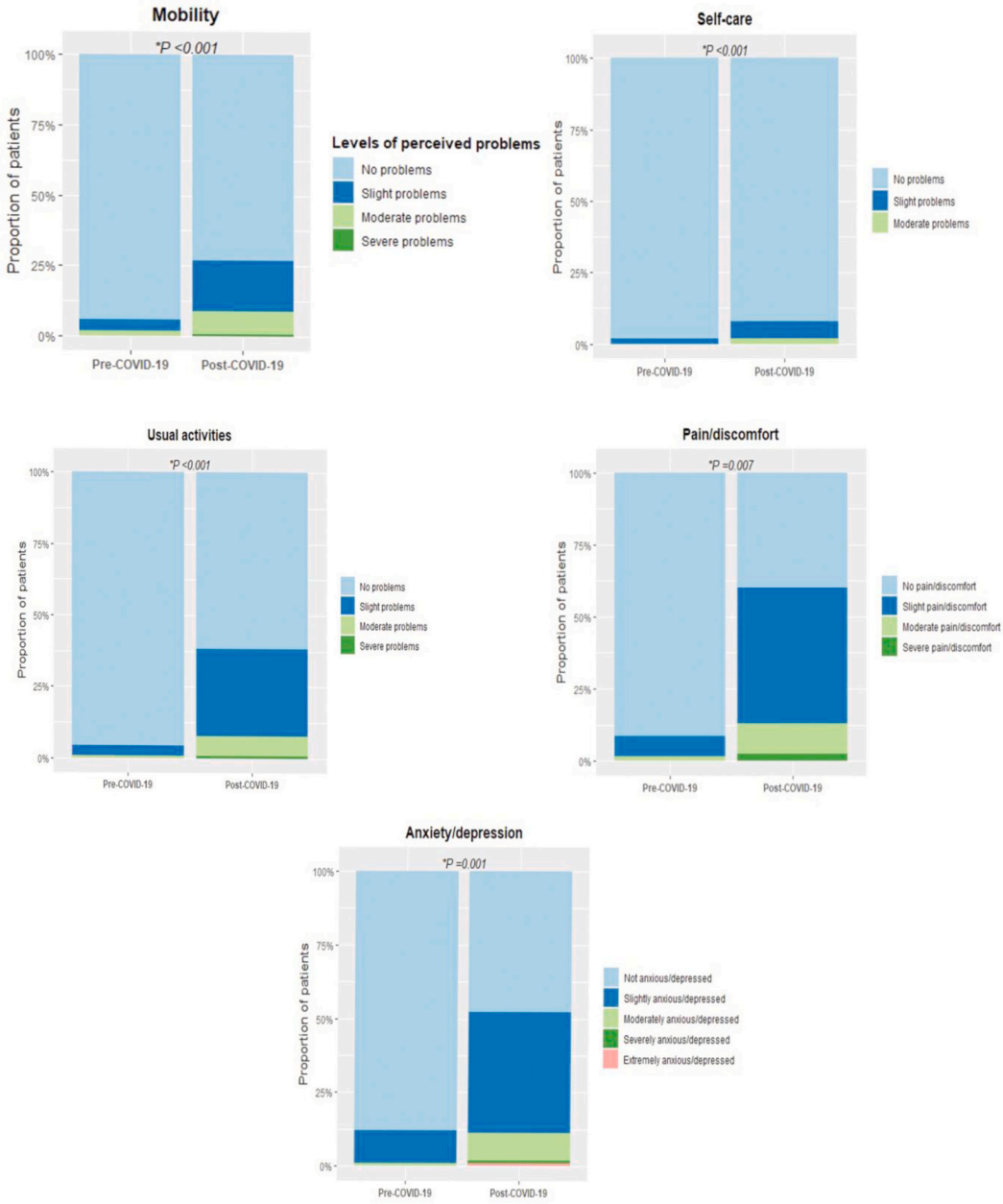

Fig. 1. Graphics showing EQ-5D-5L health state evaluation before and after COVID-19. *Statistical comparison was performed using the Mac Nemar test for paired data between no problems versus all alterations levels.

patients who had a severe decline in the EQ-5D-5L scale and who did not after COVID-19. Categorical variables were compared using the Chi-square test or Fisher's exact test, and for continuous variables, the Student *t*-test, Wilcoxon rank-sum test and signed-rank test were used. Comparations in perceived alterations pre and post COVID-19 were performed using the Mac Nemar test for paired data. Statistical significance was considered with a $P < 0.05$. All analyses were done using R Software version 3.6.3 (R-Foundation).

3. Results

Overall, 140 patients met the inclusion criteria, of whom 16 refused to participate, and 9 were excluded because of unacceptable spirometry. In the final analysis, 115 patients were evaluated, their median age was 40 years, and 57% were women (65/115). The median body mass index (27.76kg/m2) was in the range of overweight, and 27% (31/115) required hospitalization with a median length of hospital stay of 10 days (IQR, 6–12). The mean time since onset of symptoms until the evaluation was 58 ± 18 days. The persistence of symptoms was present in 63% (72/115), of whom 19% (14/72) had at least two symptoms. The median score of the EQ-5D-5L visual analogue scale pre-COVID-19 was 95 (IQR; 90–100), and after was 85 (IQR; 75–90), $P < 0.001$. There were no significant differences in the patients' baseline characteristics with a severe decline in QOL compared to those who did not have such decline, as shown in Table 1. Moreover, the frequency of spirometric alterations and persistence of symptoms did not significantly differ between both groups. However, in the severe decline group, the percentage of patients with altered ítems of health status such as usual activities and anxiety/depression were significantly higher (Table 1). All the health state parameters evaluated had a significantly higher proportion of abnormalities post-COVID-19 than pre-COVID-19, as shown in Fig. 1.

Spirometric alterations were present in 17% (20/115) of patients. All

of them had a restrictive impairment. The patients with spirometric alterations were significantly older (median of age, 48 vs. 39 years, $P = 0.003$), the presence of comorbidities such as type 2 diabetes (4/20), hypertension (3/20), smoking (4/20), overweight (10/20), and obesity (6/20) were similar in patients with and without spirometric alterations. Up to 65% (13/20) of patients with spirometric alterations had the antecedent of a mild COVID-19 disease, which was significantly higher than in the patients without spirometric alterations (32% [30/95]), $P = 0.01$. However, the former patients had a higher proportion of bilateral consolidations in the chest CT (25% [5/20]) vs. 3% [3/95], $P = 0.02$), which was performed early from symptom onset (median 4 days; IQR, 1–7). The mean of FEV1% (79.2 ± 8), PEF% (91 ± 17), FEF 25–75% (98 ± 21) and FVC% (73 ± 7) was lower than the patients with no spirometric alterations (99 ± 10, 106 ± 19, 109 ± 26 and 97 ± 11, respectively). An FEF 25–75 < 65% was present in 2/115 patients, one with a restrictive pattern. PEF<80% was present in 12/115 patients, of whom five had a restrictive pattern. The median score of the QOL visual analoge scale was lower in the post-COVID-19 period than in the pre-COVID-19 period in both groups with (median 80 vs. 95, $P < 0.001$) and without (median 85 vs. 95, $P < 0.001$) alterations in the spirometry. However, the median score in the post-COVID-19 period was significantly lower in patients with spirometric alterations than without these (median 80 vs. 85, $P = 0.02$).

4. Discussion

In this follow-up study of recovered COVID-19 patients, we found a high proportion of patients with a decrease in QOL, and this finding seemed not to have a relation with the disease severity and the persistence of symptoms. Moreover, alteration in health parameters such as usual activities and anxiety/depression were present. Restrictive impairment was the most common spirometric alteration even after mild COVID-19, and these patients had a higher decrease in QOL.

An Italian study of patients recovered from COVID-19, which included 72% of patients with pneumonia with only 20% requiring mechanical ventilation, reported a worsened QOL in 44% of patients and persistent symptoms in 87% [1]. In addition, neurocognitive sequels have recently been reported in case series of patients from Virginian, USA, who required intensive care attention [5]. Of note, 73% of our study group were outpatients, and there was a significant worsening in all the parameters of QOL and a high proportion of persistent symptoms even in mild or moderate disease.

Spirometric alterations as sequels of the Middle East respiratory syndrome have previously been related to the disease severity [2]. We found a high proportion of restrictive impairment and only a minority with small-airway dysfunction. Moreover, there was no relationship between lung function test and the severity of illness, although the antecedent of bilateral consolidations on CT was predominant in patients with spirometric alterations. Mo et al. [6], evaluated the spirometric patterns of post-COVID-19 patients, finding 9% of them with restrictive impairment associated with the disease severity. A recent Chinese study [7] found in cases of prior severe COVID-19 up to 33% of a restrictive pattern and in 16% small airway dysfunction; however, in that study, there were no significant differences in comparison with prior mild disease. These findings suggest that the severity of disease or CT alterations are not the only factor associated with impairment of respiratory function [8].

This study's limitations include the absence of pre-COVID-19 spirometry, the inclusion of patients with obesity and diabetes that might already have restrictive lung impairment and a decreased QOL. However, these comorbidities were present in the same proportions in the group with and without spirometric alterations and with and without severe decrease in QOL. The incomplete respiratory tests, the patient's heterogeneity, the retrospective evaluation of the medical records and the lack of adjustment by multiple confounders avoided obtaining definitive conclusions.

In conclusion, post-COVID-19 alterations comprised a decrease in QOL, persistent symptoms and lung function impairment. All the latter are in concordance with the called "long-haulers" [9], or "post--COVID-19 syndrome" [10] who are beginning to be recognized. We hope this study provides insights into this new disease and promotes intervention trials such as early respiratory rehabilitation and psychosocial support to improve post-COVID-19 outcomes.

Conflict of interest disclosures

None reported.

Additional information

The study was approved by the local Review Board (number, R-2020-3501-158).

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Specific author contributions

Drs. Ordinola and Lopez Luis had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. **Conceptualization and Methodology:** Ordinola, Cervantes, Cobos, Ávila, Hérnandez, Peralta Lopez Luis. **Acquisition, analysis, or interpretation of data:** Ordinola, Cervantes, Cobos, Ávila, Hérnandez, Pérez, González, Lopez Luis. **Writing - Original Draft**: Ordinola, Cervantes, Cobos, Hérnandez, Lopez Luis. **Writing - Review & Editing:** Cobos, Avila, Perez, González, Vera. **Formal analysis:** Ordinola, Lopez Luis. **Supervision and visualization**: Peralta, Vera.

References

[1] A. Carfì, R. Bernabei, F. Landi, For the gemelli against COVID-19 post-acute care study group. Persistent symptoms in patients after acute COVID-19, J. Am. Med. Assoc. 324 (6) (2020) 603–605, https://doi.org/10.1001/jama.2020.12603.

[2] L. Xie, Y. Liu, Y. Xiao, Follow-up study on pulmonary function and lung radiographic changes in rehabilitating severe acute respiratory syndrome patients after discharge, Chest 127 (2005) 2119–2124.

[3] Brian L. Graham, et al., Standardization of spirometry 2019 update. An official American thoracic society and European respiratory society technical statement, Am. J. Respir. Crit. Care Med. 200 (8) (2019) e70–e88, https://doi.org/10.1164/rccm.201908-1590ST.

[4] EuroQol Research Foundation, EQ-5D-5L user guide. https://euroqol.org/publications/user-guides, 2019.

[5] C. Ramani, E.M. Davis, J.S. Kim, J.J. Provencio, K.B. Enfield, A. Kadl, PostIntensive care unit COVID-19 outcomes-a case series, Chest (2020), https://doi.org/10.1016/j.chest.2020.08.2056.

[6] X. Mo, W. Jian, Z. Su, M. Chen, H. Peng, P. Peng, C. Lei, R. Chen, N. Zhong, S. Li, Abnormal pulmonary function in COVID-19 patients at time of hospital discharge, Eur. Respir. J. 55 (6) (2020) 2001217, https://doi.org/10.1183/13993003.01217-2020. PMID: 32381497; PMCID: PMC7236826.

[7] J. ou, L. Zhang, M.Y. Ni-Jia-Ti, J. Zhang, F. Hu, L. Chen, Y. Dong, K. Yang, B. Zhang, S. Zhang, A normal pulmonary function and residual CT abnormalities in rehabilitating COVID-19 patients after discharge, J. Infect. 81 (2) (2020) e150–e152, https://doi.org/10.1016/j.jinf.2020.06.003. Epub 2020 Jun 05. PMID: 32512021; PMCID: PMC7273134.

[8] Y. Huang, C. Tan, J. Wu, M. Chen, Z. Wang, L. Luo, X. Zhou, X. Liu, X. Huang, S. Yuan, C. Chen, F. Gao, J. Huang, H. Shan, J. Liu, Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase, Respir. Res. 21 (1) (2020) 163, https://doi.org/10.1186/s12931-020-01429-6. PMID: 32600344; PMCID: PMC7323373.

[9] R. Rubin, As their numbers grow, COVID-19 "long haulers" stump experts, J. Am. Med. Assoc. (2020), https://doi.org/10.1001/jama.2020.17709. Epub ahead of print.

[10] Y.M.J. Goërtz, M. Van Herck, J.M. Delbressine, A.W. Vaes, R. Meys, F.V. C. Machado, S. Houben-Wilke, C. Burtin, R. Posthuma, F.M.E. Franssen, N. van Loon, B. Hajian, Y. Spies, H. Vijlbrief, A.J. van 't Hul, D.J.A. Janssen, M.A. Spruit, Persistent symptoms 3months after a SARS-CoV-2 infection: the post-COVID-19 syndrome? ERJ Open Res (2020), 00542-2020. doi: 10.1183/23120541.00542-2020. PMCID: PMC7491255.